

Inderal*

DOSAGE AND ADMINISTRATION ORAL

Angina Pectoris

Initially, 20 mg, three to four times daily, before meals and at bedtime. Thereafter, and over the course of one week, dosage should be increased gradually to 40-60 mg, three to four times daily. Occasionally, doses as high as 320-400 mg have been administered safely with beneficial results to patients with resistant angina, but such doses are not generally required.

Arrhythmias 10-30 mg three or four times daily, before meals and at bedtime.

Hypertrophic Subaortic Stenosis 20-40 mg, three or four times daily, before meals and at bedtime.

Phaeochromocytoma

Preoperatively — 60 mg daily, in divided doses, for three days prior to surgery, concomitantly with an alpha-adrenergic receptor blocking agent.

Malignant cases — 30 mg daily, in divided doses.

INTRAVENOUS

Cardiac Arrhythmias

1-3 mg, at a rate of 1 mg (1 ml) per minute. A similar dose may be repeated after two minutes, depending upon the response.

Note: Usual dosage of 1-3 mg should be administered under ECG monitoring wherever practicable. The rate of administration should not exceed 1 mg (1 ml) per minute. Sufficient time should be allowed to enable a slow circulation to carry the drug to the site of action. Once an alteration in rate or rhythm is noted, it is advisable to give no further Inderal until the full effect is observed.

Depending upon the response, a second dose may be repeated after two minutes. Additional medication should not be given unless it is clear that the desired therapeutic effect has not been achieved and no adverse effects, particularly bradycardia or congestive heart failure, have occurred. In the therapy of cardiac arrhythmias, it is seldom necessary to give doses greater than 10 mg intravenously.

Should excessive bradycardia occur, atropine 0.5 to 1.0 mg should be administered intravenously.

CONTRAINDICATIONS

1. Bronchial Asthma

2. Allergic Rhinitis (during pollen season)

3. Sinus Bradycardia (and greater than second degree or total heart block)

On occasion, the administration of Inderal has resulted in sinus bradycardia due to unopposed vagal activity and has been corrected by atropine.

4. Cardiogenic Shock

5. Right Ventricular Failure (secondary to pulmonary hypertension)

6. Congestive Heart Failure

Predictably, Inderal may worsen frank congestive failure. While the correction of a major arrhythmia may decrease congestive failure, and Inderal intravenously has been useful in this application, prior digitalization should be combined with small doses of Inderal, repeated only if indicated and carried out under constant electrocardiographic monitoring. Inderal does not abolish the positive inotropic action of digitalis glycosides.

Patients without a history of cardiac failure have also occasionally developed failure, or patients in incipient failure have developed overt congestive failure after treatment with Inderal. In such cases, the action taken will depend on the response of the patient to Inderal. If unsatisfactory, Inderal should be stopped immediately. If the response is good, patients should be fully digitalized and observed closely. If failure persists, Inderal should be withdrawn completely. The number of patients presenting difficulties of this kind is small in relation to the total number treated.

7. Chloroform and Ether Anesthesia

NOTE: FOR PRECAUTIONS AND ADVERSE REACTIONS: See Scientific Brochure.

AVAILABILITY

No. 3461, Inderal 10 mg, in bottles of 100 buff-colored, scored tablets.

No. 3464, Inderal 40 mg, in bottles of 100 green, scored tablets.

No. 3265, in 1 ml ampuls containing 1 mg, packed in cartons of 10.



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MEMBER

PMAC

CORRESPONDENCE

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and immunosuppressive drugs is now possible.

The most likely cause of decreased vision in either eye in the case reported would seem to be a vascular occlusion.

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Psychosis induced by oral contraception

To the Editor:

While oral contraceptives provide excellent conception control and separate in time and body locale the means of contraception and the sexual act, they have been held responsible for a number of undesirable side effects. Carefully collected evidence suggests an association of emotional changes,¹⁻³ but the relationship of these to the patient's personality structure and neuroticism is far from clear. Psychotic reactions upon withdrawal of estrogen-progesterone have been reported by Keeler et al⁴ and Idestrom⁵ and cases with its use by Daly et al,⁶ Sturgis⁷ and Kane et al.⁸ Most of these cases occurred in women who had suffered from previous postpartum psychosis and character disorder.

We wish to report a case of schizophreniform psychosis induced by oral contraception in a patient who had had no previous psychiatric disability.

The patient was a 25-year-old white married woman with two children aged 5 and 2 years and had had two miscarriages. She had practised contraception by observing the safe period or by condom. She was prescribed Miniquen, a sequential oral contraceptive agent (mestranol 0.1 mg., ethynodiol diacetate 0.5 mg., G. D. Searle and Co.) in May 1970. Soon afterward she started feeling nervous, irritable, depressed and easily fatigued, and noticed loss of libido. She neglected her housework and thought that other people were going to take her children away as she was not looking after them properly. Gradually her symptoms became worse; she told her husband that the neighbours were talking about her and were against her. Both she and her husband felt that the birth control pill was responsible for these changes.

When she complained to her general practitioner at the end of June and asked if she could use a diaphragm instead, she was advised to continue the pill and was prescribed butabarbital sodium, 15 mg. four times daily. This reduced slightly her anxiety, depression, paranoid ideas and hallucinations for a short while. Later she started accusing her husband of not loving her any more, became scared of sexual relations and moved her bed to a separate room. Her appetite decreased and she lost weight. She became excessively religious and prayed at inappropriate times and in inappropriate places. Marital friction increased and she asked her husband for a separation. In the

first week of August she took a job to be self-sufficient and at work it was noticed that she frequently laughed or cried for no obvious reason, remained aloof and performed her work inadequately. Her doctor changed her from Miniquen to a combined-type contraceptive pill.

She was seen for psychiatric evaluation on August 27. She came for the interview quite willingly and although she giggled at intervals, she gave a coherent account of her problems. Three times during the interview she got up to investigate objects in the room, looked at the notebook in which her history was being recorded and walked about. She remained polite and compliant but the giggling became more frequent. She was admitted to hospital and further observation revealed periods of restlessness, frequent mood swings, smiling to herself and occasionally responding to the auditory hallucinations she admitted. On occasion she knelt and prayed in corridors, bedroom and sitting room. She displayed a marked degree of incoherence and thought disturbance at times. She expressed paranoid ideas about her neighbours and strange ideas about religion. There was evidence of scattering, general disorganized thinking, mild degree of blocking, poor body image and marked tendency to predominantly concrete thinking.

In the past she had enjoyed good health except for a mild degree of diabetes which was discovered during her second pregnancy and was controlled by the use of Mobenol. Family history revealed that her father had suffered from depression while chronically ill from heart disease prior to his death at the age of 58. One paternal uncle suffered from a short period of depression at the age of 55 and was treated in this unit.

The contraceptive pill was immediately discontinued and pyridoxine, 100 mg. t.i.d. was prescribed. She was first given thioridazine which, because of the drowsiness and unsteady gait it induced, was changed on August 31 to trifluoperazine, 5 mg. t.i.d. She also received benzhexol, 2 mg. t.i.d. later increased to 5 mg. for control of extrapyramidal side effects. She improved slightly but her breasts became markedly engorged and tender and there was lactation. When her medication was stopped this side effect settled promptly. She received a short course of ECT to hasten her recovery. She was discharged on September 19, 1970, on no medication. Since her discharge she has managed very well. She was fitted with an IUD and marital relations are normal and family life is well adjusted and happy. She was discharged from outpatient psychiatric follow-up care on January 12, 1971 while completely symptom-free.

There is now a sufficient body of evidence to establish a relationship between the use of oral contraceptives and the occurrence of emotional changes. The relationship is complex and not yet completely understood. These side effects can have serious consequences for a patient and her family, and therefore their early recognition is important. Some women are at a greater risk than others, namely those who have suffered from postpartum disturbance, depressive illness or premenstrual depression. Before prescribing oral contraceptives the routine examination should in-

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clude an assessment of mood. Emotional changes should be looked for, as many women will not volunteer such information.

It is possible that psychosis due to oral contraceptives is produced by the same biochemical changes which follow the use of steroid hormones of many kinds and which are known to lead to occasional psychotic breakdown.⁸ The use of estrogen is always accompanied by a rise of plasma corticosteroids.⁹ The majority of investigators, though not all, believe that these exist in a bound or inactive form; however, one report¹⁰ indicates that by the use of advanced measuring techniques a 2½-fold increase in unbound steroids exists at the tissue level.

Synthetic progestogens are also known to influence cerebral activity, and it has been demonstrated that women taking estrogen-progesterone preparations have greatly increased urinary levels of tryptophan metabolites such as 3-hydroxy-anthranilic acid. On the basis of this finding it is suggested that levels of 5-hydroxytryptamine in the brain are affected and lead to emotional changes. On the assumption that pyridoxine may influence the metabolic fate of 3-hydroxy-anthranilic acid in the tryptophan-niacine pathway, its use in prophylaxis of emotional changes has been advocated. Baublatt and Winston¹¹ recommend further research following their encouraging results in the treatment of mood changes with pyridoxine.

It is possible that our patient was more vulnerable owing to relative pyridoxine deficiency because of her diabetes. On theoretical grounds we would suggest that extra attention should be paid to patients on oral contraceptives who suffer from conditions rendering them relatively pyridoxine-deficient, e.g. diabetes mellitus, chronic alcoholism, malnutrition and treatment with isoniazid and cycloserine etc.

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Making cholestyramine palatable

To the Editor:

Since my review article "Cholestyramine" was published in the *Journal (Canad Med Ass J 104: 305, 1071)*, I have received several comments on how difficult it is to administer the drug to patients. Of undoubted benefit to many people, to some it appears that the cure is worse than the disease.

There are two commercial preparations available in Canada, Cuemid and Questran. Unfortunately both can be obtained only as a dry powder. Capsules have not been practical in the past because of the large volume of the drug required in most conditions. The low volume of potential sales for the resin and the difficulties in getting new dosage forms approved by the Food and Drug Directorate have stood in the way of more palatable preparations. Questran tends to disperse better in an aqueous solution than Cuemid and for this reason is generally preferred by most patients. Taste and odour bother some patients while others claim that it is odourless and tasteless but that it is the grittiness that distresses them. A No. 00 gelatin capsule will hold approximately 0.5 g. of the powder (i.e., 0.25 g. of cholestyramine resin) but the capsule must be filled by the patient himself.

Faced with these difficulties, some of our more ingenious patients have devised recipes which hide the drug and reduce its gritty sensation. Aqueous solutions tend to be absorbed by the drug, which then swells and increases in bulk. Oily substances, on the other hand, blend with the resin, disguising its grittiness and making it easier to swallow. Although fatty acids are weakly bound to cholestyramine,¹ they apparently do not interfere with its efficacy in patients who have choleretic diarrhea.

The following are examples of recipes suggested by patients:

1. Mix the drug into 2 tablespoonfuls (more or less as desired) of mayonnaise or salad dressing and press the mixture into the groove of a large celery stalk. The mixture will be more translucent than plain mayonnaise, and if desired a little more plain mayonnaise could be spread over the mixture in the groove. The crispness of the celery will mask the grittiness of the powder and detract from any noticeable bitterness.

2. Make a cheese sauce—any of several ways:

- (a) Use a white sauce base (flour, melted margarine and milk) and add shredded cheddar cheese after the white sauce has cooled a bit.

- (b) Gently melt processed cheese slices or "Cheese Please" or "Cheese Whiz" in milk, using low heat and a heavy saucepan or a double boiler.

Mix the drug into 2 tablespoonfuls (more or less as desired) of the cheese sauce and pour over lightly cooked broccoli or mashed hot potatoes to be eaten with fresh parsley, celery or crisp green peppers.

3. Mix the drug into 2 tablespoonfuls (more or less as desired) of peanut butter and make a small sandwich with bread or buttered toast and eat with crisp green lettuce or celery.

4. Add to hot tea or coffee with about 2 teaspoonfuls of condensed milk.

5. Add to desired amount of prepared concentrated fresh orange juice.

Obviously, there are many other ways of taking the drug, but powdered cholestyramine will never be a gourmet's delight and the firm that provides a palatable preparation will be doing a service to the patients who use this drug.

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Reference

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Dietary sugar and myocardial infarction

To the Editor:

We North Americans eat so much sugar in one way or another that it would be reassuring to know that our collective sweet tooth did not predispose us to myocardial infarction. Anyone who is prompted to believe as Dr. Gilder suggests (*Canad Med Ass J 104: 286, 1971*) that the hypothesis implicating high dietary sucrose has finally "bitten the dust" should read Professor Yudkin's recent letter "Sugar Consumption and Myocardial Infarction" in the *Lancet* of February 6 (p. 296).

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Letters are welcomed and will be published, if suitable, as space permits. They should be typewritten, double-spaced.